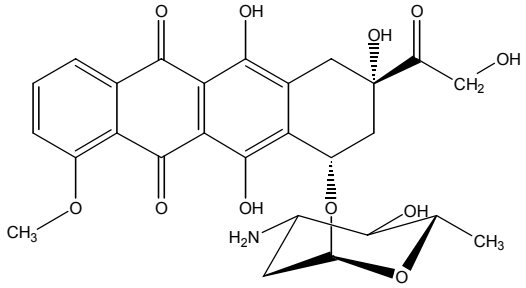
ADRIAMYCIN® (DOXORUBICIN HYDROCHLORIDE)
CAS No. 23214-92-8
First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

Adriamycin® is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.10, 1976; IARC S.4, 1982). A single intravenous injection of Adriamycin® induced mammary tumors in female rats. Intravesicular instillation of Adriamycin® in rats resulted in a low incidence of bladder papillomas and enhanced the incidence of urinary bladder tumors induced by *N*-nitroso-*N*-(4-hydroxybutyl)-*N*-butylamine. Single or repeated subcutaneous injections induced local sarcomas in rats.

There is inadequate evidence for the carcinogenicity of Adriamycin® in humans identified (IARC V.10, 1976; IARC S.4, 1982; IARC S.7, 1987). No epidemiological study of Adriamycin® alone was available for review. However, in one study of cancer patients receiving Adriamycin® in combination with alkylating agents and radiotherapy, the patients developed leukemia and bone cancer (IARC S.4, 1982).

PROPERTIES

Adriamycin® is the hydrochloride of doxorubicin (14-hydroxydaunomycin). It is a red, crystalline solid with a melting point of 204 °C. It is soluble in water and aqueous alcohols, moderately soluble in anhydrous methanol, and insoluble in nonpolar organic solvents. Neutral aqueous solutions of Adriamycin® are stable when stored at 5°C. When heated to decomposition, Adriamycin® emits toxic fumes of nitrogen oxides (NO_x) and hydrogen chloride.

USE

Adriamycin® is a cytotoxic anthracycline antibiotic used in antimitotic chemotherapy. It is infused intravenously to treat neoplastic diseases such as acute lymphoblastic leukemia, Wilm's tumor, soft tissue and osteogenic sarcomas, Hodgkin's disease, non-Hodgkin's lymphomas, Ewing's sarcoma, and bronchogenic, genitourinary, breast, and thyroid carcinoma (IARC V.10, 1976).

PRODUCTION

Adriamycin® is no longer produced domestically, but it is imported from Italy (PDR, 1995). No import volumes, however, are available. Italy and Japan are the only known producers of adriamycin (IARC V.10, 1976). The *1998 Chemical Buyers Directory* lists three U.S. suppliers of the compound (Tilton, 1997).

EXPOSURE

The primary routes of potential human exposure to Adriamycin® are injection, dermal contact, and inhalation. The recommended dosage schedule for adult patients is 60-75 mg/m^2 body surface as a single intravenous infusion at 21-day intervals until a total of 550 mg/m^2 is given (IARC V.10, 1976). Health professionals who handle this drug (for example, pharmacists, nurses, and physicians) may be exposed during drug preparation, administration, or cleanup. Potential occupational exposure may also occur through inhalation and dermal contact for workers involved in manufacturing Adriamycin®. The National Occupational Exposure Survey (1981-1983) estimated that a total of 17,133 workers, including 11,918 women, potentially were exposed to Adriamycin® (NIOSH, 1984). Although Adriamycin® is used in relatively small quantities, there is a small pollution problem relative to hospital wastes. However, the risks can be avoided through use of appropriate containment equipment and work practices (Zimmerman et al., 1981).

REGULATIONS

FDA regulates Adriamycin® under the Food, Drug, and Cosmetic Act (FD&CA) as a prescription drug approved for human use. FDA has ruled that Adriamycin® must carry a warning label regarding potential carcinogenicity, mutagenicity, teratogenicity, and/or impairment of fertility. OSHA regulates Adriamycin® as a chemical hazard in laboratories under the Hazard Communication Standard. Regulations are summarized in Volume II, Table B-5.